

REMARKS

In the Office Action dated September 5, 2007, the Examiner rejected all of the pending claims as anticipated by Tuschl (WO 02/44321 A1). Applicants respectfully submit that the Examiner misapplied the novelty standard and that when the pending claims are reviewed under the appropriate standard, they should be deemed patentable over the art of record.

The Pending Claims, Amendments and Applicants' Invention

The pending claims are directed to new and non-obvious methods for obtaining siRNA molecules and methods for selecting siRNA sequences. Through the use of these methods one can obtain a particular siRNA that is more likely to be functional than an siRNA sequence that is selected or an siRNA molecule that is obtained at random.

Applicants note that each independent claim requires an affirmative step of applying one or more specific criteria, then selecting a candidate based on those criteria and either synthesizing the siRNA molecule or outputting an siRNA sequence. (See *e.g.*, claims 1, 43, 68, 61, and 86, step (c) – (e)). Thus, in the pending claim set, Applicants do not herein claim compositions that satisfy the recited criteria. Instead, they claim methods in which one affirmatively applies, selects and either synthesizes or outputs based on the application of the criteria. This is a new and more efficient method of reaching a result.

Applicants have amended claims 1, 38-43 and 61-66, 68 and 86. Claims 1 and 61, and the claims that depend on them are directed to methods for selecting and obtaining an siRNA molecule and methods for selecting an siRNA sequence that require the application of a criterion that looks at the thermodynamic principles of the two ends of the duplex region through the comparison of the number of A and U nucleotides at the different ends of the duplexes. Through the amendments to the claims, Applicants have made explicit what was implicit, that when comparing the number of A and U nucleotides one does not consider overhang regions of an siRNA duplex if present.

Support for these amendments may for example be found in paragraphs: [0212] directing consideration of “low internal thermodynamic stability of the duplex at the 5'-ant sense (AS)”; [0214] noting that when considering GC content one does not consider overhangs; and [0237] noting “the frequency of A/U bp was determined for each of the five terminal positions of the duplex”

Applicants have similarly amended claims 43, 68 and 86 to make explicit what was implicit, and added language to note that a duplex region of 19 – 30 base pairs is formed and that the positions are referenced with respect to the 5' end of the antisense sequence (or region) within the duplex. Support for these amendments may for example be found in paragraphs [0099] referring to references being made within the 5' of the duplex; [0214] noting that position 15-19 are within the duplex; and [0232] noting that the frequency of the nucleotides within the duplexes was analyzed.

Applicants have also deleted an extra occurrence of the word “and” in each of claims 1 and 43. No new matter has been added.

Response to Rejection Under 35 U.S.C. § 102(a)

“Cases involving novelty, with its strict identity requirement, are quite rare.” *Trintec v. Top-U.S.A.*, 295 F.3d 1292, 1297 (Fed. Cir. 2002). A rejection under 35 U.S.C. § 102(a) is appropriate if and only if a prior art reference discloses all of the limitations of a claim. *In re Cruciferous Sprout*, 301 F.3d 1343, (Fed. Cir. 2002), *cert. denied*, 538 U.S. 907 (2003); *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (“It is axiomatic that anticipation of a claim under § 102 can be found only if the prior art reference discloses every element of the claim . . .”).

When a method or process is claimed, in order for a claim to have been anticipated, each step of the method or process must be described or embodied in a single reference, *Glaverbel Societe Anonyme v. Northlake Marketing*, 45 F.3d 1550, 1554 (Fed. Cir. 1995), and “it is incumbent upon the Examiner to identify wherein each and every facet of the claimed invention is disclosed in the applied reference.” *Ex Parte Levy*, 17 U.S.P.Q. 2d. 1461, 1462 (Bd. Pat. App. Int. 1990); see also *Gerhard Gross v. Vincenzo Spitaleri*, 2002 Pat. App. LEXIS 218 (Bd. Pat. Int.) (“We note that the initial burden of presenting a prima facie case of unpatentability on any ground rests with the examiner.”).

“The absence of even one limitation recited in a claim from a prior art reference is enough to negate anticipation by that reference.” *Louisville Bedding Co. v. Pillowtex*, 1997 U.S. Dist. LEXIS 24023 (W.D. Ky. Aug. 19, 1997).

The Examiner points to Tuschl’s disclosure of certain synthesized siRNA duplex structures as anticipatory of pending claims. Applicants respectfully submit that although the Examiner has cited an example of siRNA that meets certain of the specified criteria, the Examiner has not shown that the reference teaches to apply the recited criteria. In the absence of pointing to where the reference teaches elements (c) –(e) of each of the independent claims, Applicants respectfully submit that the Examiner has not met her burden of making a *prima facie* case of novelty.

To the extent that the Examiner implies that Tuschl inherently discloses Applicants’ claimed invention, Applicants’ respectfully submit that the Examiner’s reliance on this doctrine is improper. In order to rely on the theory of inherency, an examiner must offer a basis in fact and/or technical reasoning that reasonably supports the determination that an allegedly inherent characteristic necessarily flows from the teaching of an applied prior art reference. *Ex. Parte Richard Brothers*, 2002 Pat. App. LEXIS 297 (Bd. Pat. App. Int.) “Inherency ‘may not be established by probabilities or possibility. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.’” *Id.* (quoting *Ex parte Skinner*, 2 U.S.P.Q.2d 1788, 1789 (Bd. Pat. App. & Int. 1986)); *Crown Operations v. Solutia*, 289 F.3d 1367, 1377 (Fed. Cir. 2002) (the mere fact that a certain thing may result from a given set of circumstances is not sufficient”).

Had Tuschl used Applicants’ selection criteria, he may have selected the siRNA as cited by the Examiner. However, that he could have used these criteria does not render his patent application an inherent disclosure of these selection criteria. Applicants reemphasize that they have not claimed an siRNA molecule or sequence, wherein a criterion is met. Instead they have claimed methods for selecting and obtaining siRNA sequences and molecules and thus applying and selecting based on certain criteria. Thus,

Applicants have invented a new method of doing business – a new method based on bioinformatics. That the end result is the selection of a known sequence, does not detract from the patentability of the method to select it. New methods for obtaining a known product have long been recognized as patentable, and because Applicants' method is such a new method that might be used to select and obtain a known sequence, the method is patentable. *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998) (patentability of business methods are held to same standards of patentability under 35 U.S.C. §§ 102 and 103), *cert. denied*, 595 U.S. 1093 (1999).

Applicants further respectfully submit that in the very parts of Tuschl to which the Examiner points, Tuschl suggests using selection criteria other than those claimed by the Applicants. Tuschl's example 3 is directed to *Specific Inhibition of Gene Expression by RNA Interference*. In that example, Tuschl synthesized five 21-nt sense siRNAs, each displaced by one nucleotide relative to the target RNA and eight 21-nt antisense siRNAs each displaced by one nucleotide relative to the target. (pages 43 – 44 of Tuschl) Thus, Tuschl selected his siRNA by a walk along the target sequence, not based on any selection criteria. Accordingly, Tuschl does not disclose Applicants' claimed methods.

Moreover, in this example, Tuschl introduced the variable of overhang size and concluded: "The ability of 21-nt siRNA duplexes to mediate RNAi is dependent on the number of overhanging nucleotides or base pairs formed." (page 43 of Tuschl) He concludes that 2-nt 3' overhangs were most efficient. *Id.* Nowhere does Tuschl disclose Applicants' recited criteria. Because Tuschl does not teach Applicants' recited criteria, he does not teach methods for applying these criteria. Accordingly, Applicants respectfully request that the outstanding rejection be withdrawn.

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Applicants submit that no fee is necessary with the Response. However, if any fee is deemed necessary, Applicants authorize the Patent Office to charge the Deposit Account No. 11-0171 for any such sum.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Scott D. Locke', is written over a horizontal line.

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